SM.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,739	07/31/2001	William J. Egan	PHARMA.003A	3949

20995 7590 04/14/2004

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/919,739	EGAN ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4 and 6-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,and 6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/12/04 has been entered.

Claims herein under examination are 3,4, and 6-8.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3-4 and 6-8 are rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter. As written, claims 3-4 and 6-8 encompass a method performed on a computer that appears to lack any physical result performed outside of a computer.

As stated in MPEP § 2106, (IV)(B)(2)(b), to be statutory, a claimed computer-related process must either: (A) result in a physical transformation outside the computer for which a practical application in the technological arts is either disclosed in the specification or would have been known to a skilled artisan (discussed in MPEP § 2106 (IV)(B)(2)(b)(i)), or (B) be limited to a practical application within the technological arts (discussed in MPEP § 2106 (IV)(B)(2)(b)(ii)).

As stated in MPEP § 2106 (IV)(B)(2)(b)(i), the independent physical acts may be post- or pre-computer processing activity as described below:

> A process is statutory if it requires physical acts to be performed outside the computer independent of and following the steps to be performed by a programmed computer, where those acts involve the manipulation of tangible physical objects and result in the object having a different physical attribute or structure. Diamond v. Diehr, 450 U.S. at 187, 209 USPQ at 8. Thus, if a process claim includes one or more post-computer process steps that result in a physical transformation outside the computer (beyond merely conveying the direct result of the computer operation), the claim is clearly statutory.

> Another statutory process is one that requires the measurements of physical objects or activities to be transformed outside of the computer into computer data (In re Gelnovatch, 595 F.2d 32, 41 n.7, 201 USPQ 136, 145 n.7 (CCPA 1979) (data-gathering step did not measure physical phenomenon); Arrhythmia, 958 F.2d at 1056, 22 USPQ2d at 1036), where the data comprises signals corresponding to physical objects or activities external to the computer system, and where the process causes a physical transformation of the signals which are intangible representations of the physical objects or activities. Schrader, 22 F.3d at 294, 30 USPQ2d at 1459 citing with approval Arrhythmia, 958 F.2d at 1058-59, 22 USPQ2d at 1037-38; Abele, 684 F.2d at 909, 214 USPQ at 688; In re Taner, 681 F.2d 787, 790, 214 USPQ 678, 681 (CCPA 1982).

As stated in MPEP § 2106 (IV)(B)(2)(b)(ii), the computer-related process may be limited to a practical application in the technological arts as described below:

> There is always some form of physical transformation within a computer because a computer acts on signals and transforms them during its operation and changes the state of its components during the execution of a process. Even though such a physical transformation occurs within a computer, such activity is not determinative of whether the process is statutory because such transformation alone does not distinguish a statutory computer process from a nonstatutory computer process. What is determinative is not how the computer performs the process, but what the computer does to achieve a practical application. See Arrhythmia, 958 F.2d at 1057, 22 USPQ2d at 1036.

Claims 3-4 and 6-8 do not fulfill either of these statutory requirements and are therefore rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

Claims 3-4 and 6-8 are rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter. As written, the claims appear to be directed to a method that

merely manipulates numbers, abstract concepts or ideas, or signals representing any of the foregoing.

As stated in MPEP § 2106, (IV)(B)(1), if the "acts" of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. Schrader, 22 F.3d at 294-95, 30 USPQ2d at 1458-59. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process.

In practical terms, claims define nonstatutory processes if they:

> – consist solely of mathematical operations without some claimed practical application (i.e., executing a "mathematical algorithm"); or
> – simply manipulate abstract ideas, e.g., a bid (Schrader, 22 F.3d at 293-94, 30 USPQ2d at 1458-59) or a bubble hierarchy (Warmerdam, 33 F.3d at 1360, 31 USPQ2d at 1759), without some claimed practical application.

Claims 3-4 and 6-8 do not fulfill any of these statutory requirements and are therefore rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

Applicants submit that amended claims 3-4 and 6-8 are directed to statutory subject matter because they disclose manipulating data representing physical objects. This is found unpersuasive as the instant invention appears to merely be a data manipulation process. The fact that the data may represent physical objects does not nullify this rejection as the data manipulation process contains no physical element to it outside of the computer. Applicants state that receiving data of molecules must be obtained from the physical world. This is found unpersuasive as amended claim 3 does not decisively state that this step is taking place in the

physical world outside of the computer. In contrast, amended claim 3 can be reasonably interpreted to be receiving data from or within a computer or via the internet, for example.

Claims Rejected Under 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF WRITTEN DESCRIPTION

Claims 3-4 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

The support provided by Applicants for the phrase "receiving data" (page 5 [lines 10-31] and page 14 [lines 3-15] of the specification) does not appear to give adequate written basis to support this added phrase. The section of page 5 of the specification states a property is determined and reference molecules are classified. This section makes no reference as to whether these molecular data were already present or newly received. Applicants state that in order for the classifying step to occur, the data must be provided and "received". This is found unpersuasive as there is no evidence that the data were not already present.

The support provided by Applicants for the phrase "choosing said first molecule as a marker molecule if said first molecule has" (page 10 [lines 3-5 and 11-14] and page 11 [lines 13-16] of the specification) does not appear to give adequate written basis to support this added

phrase. These passages do not mention any first molecules. Applicants state that in order to define a set of markers, individual molecules must be separately evaluated. This is found unpersuasive as this reasoning does not support why a first molecule would be chosen. Applicants state an example such as a "marker molecule set containing only Naproxen" which is found unpersuasive as there is no indication that Naproxen was the "first" molecule.

Because the introduction of phrases "receiving data" and ""choosing said first molecule as a marker molecule if said first molecule has" lacks written basis, these phrases in amended claim 3, filed 2/12/04, is considered NEW MATTER. Claims 4 and 6-8 are also rejected due to their dependency from claim 3.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-4 and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Stanton et al. (J. Chem. Inf. Comput. Sci. 1999, Vol. 39, pages 21-27).

Stanton et al. disclose that the objective of drug discovery screening computer programs is to identify hits, or a selection of molecules, to provide a preliminary understanding of the structure-activity relationship between a set of compounds and a target (page 21, col. 1, lines 1-15 and col. 2, second paragraph). Stanton et al. disclose the necessity of the program to evaluate

large databases (sets) with molecular descriptors in order to select those that produce chemistry spaces general enough to study large and diverse subsets of chemical structures and still be able to identify subtle differences between highly similar substances (page 21, col. 1, lines 25-33). Stanton et al. disclose programs that identify leads for potential drug candidates (abstract, lines 1-2) which represents a predictive model. Stanton et al. disclose receiving data relating to anti-bacterial activity (page 22, col. 1, second paragraph). For example, Stanton et al. disclose subsets of a set of compounds from a larger combinatorial library used in assays to identify compounds with antibacterial activity (page 22, col. 2, lines 11-28). Thus, the hits in these subsets function as molecular markers that are reasonably interpreted as things that mark or indicate a concept or trait, such as antibacterial activity (page 22, col. 2, lines 13-14). Stanton et al. disclose examples of various properties to examine involving protein binding such as inhibition of bacterial cell growth, metabolic pathways, and isolated enzymes (page 23, col. 2, lines 1-5) so that selected molecules which indicate the presence of these properties would be considered markers of the properties. As mentioned above, Stanton et al. disclose an example of using the property of antibacterial activity (page 22, col. 2, lines 11-14) in a study, starting with a large combinatorial library (10,000 compounds), finding 212 hits (which represents the classification of a set of reference molecules as stated in claim 3), performing a hierarchical cluster analysis (Figure 1), using a cutoff point (threshold) to yield seven subsets (which represents subset selection as stated in claim 3), and then conducting further studies on representatives in the subsets (which represents the selection of marker molecules from the subset in claim 3) (page 22, col. 2, lines 10-28). Stanton et al. disclose the use of molecular and biological descriptors when doing cluster analysis (page 22, col. 1, lines 16-24). Stanton et al.

disclose cluster analysis resulting in dendrograms which were examined visually to determine cut-off thresholds for appropriate levels of similarity (page 21, col. 2, lines 24-26 and Figure 1) to further narrow down the selection of molecules as stated in claim 3. Stanton et al. disclose the goal of producing sufficient data for each class of hits (subsets) to make decisions regarding potential leads (page 21, col. 1, lines 15-18 and page 22, col. 2, line 1), such that selection of the potential leads within the subset are the selected marker molecules as stated in claim 3. Stanton et al. disclose the cluster analysis methods provide a rapid way to reducing large sets of hits into smaller manageable structural classes (page 22, col. 2, lines 1-5). Stanton et al. disclose an example where three subsets were clearly visible in the resulting dendrogram (page 22, col. 2, lines 29-41 and Figure 2) from which compounds were selected for follow-up work from each class as stated in claim 3. Stanton et al. disclose the molecular structure descriptors were taken from BCUT metrics which form a particular chemistry space in order to perform hierarchical cluster analysis, including a similarity metric which was predefined to be based on the squared Euclidean distance (page 21, col. 2, lines 9-23) as stated in claim 3. Stanton et al. disclose the activity of five related hits and each compound's Euclidean distance from the original query (page 24, col. 1, lines 37-41). Stanton et al. disclose nearest-neighbor (NN) searches (page 21, col. 2, lines 27-29) that included the query compounds as well as the compounds from databases to calculate BCUT metrics (page 22, col. 1, lines 1-3). Stanton et al. disclose the 20-30 closest neighbors to a given query were selected from multiple databases for subsequent screening (page 22, col.1, lines 4-5) which is reasonably interpreted that the counting step was repeated producing varying results (20-30 results) as stated in claim 3. Stanton et al. disclose that the hit rate can be controlled by altering assay conditions used or setting rigorous criteria of a specific

property (i.e. 80% inhibition instead of 50%) as well as looking at a broad range of hits (page 22, col. 1, lines 32-36) which is reasonably interpreted as repeating the count process with various thresholds as stated in claims 3, 6, and 7. Stanton et al. disclose some subsets at 100% similarity in Figure 2 which represent a minimum distance as well as the most accurate of predictions as seen in the dendrogram as stated in claims 7 and 8. Stanton et al. disclose the final six best hits (markers) out of 210 compounds, which represent the most accurate hits from the original subset (Table 1 caption). Stanton et al. disclose an example of nearest neighbor analysis of a first molecule that is used to identify sets of potentially active compounds that are similar to the first molecule (page 24, col. 1, lines 29-37 and Table 1). Stanton et al. disclose in Figures 5a and 5b the sorting of molecules (210 total, see Table 1 caption) in a set in descending order of numerical similarity (based on Euclidean distance) to the original query where one can visually determine the number of molecules in between the first molecule and another molecule at a particular NN distance away as stated in claim 3. Stanton et al. disclose using active compounds as starting points (as first molecules) to screen other compounds for similarity using a threshold of <= 50 μM as the threshold cut off value (page 24, col. 2, lines 8-16). Stanton et al. disclose a fractions-correctly-predicted metric in Table 2 (last column) where the number of molecules in the range which are also part of the subset (third column) are divided by the total number of molecules in the range (second column) to give the metric expressed as a percent in the fourth column (page 25, col. 1-2 and Figure 5). Stanton et al. disclose a threshold of a NN distance of 1.9 or less in order to find a 20% hit rate (page 26, col. 1, lines 6-11).

Thus, Stanton et al. anticipate the limitations in claims 3-4 and 6-8.

Applicants state claim 3 explicitly defines "fractions-correctly-predicted metric as the number of molecules in said range which are also members of said subset divided by the total number of molecules in said range". This is acknowledged. Applicants also state the "range" in this limitation is the "range in molecules of similarity of similarity distance away from" the "first molecule". This is acknowledged. Applicants state Stanton et al. do not disclose similarity distances in Table 2, let alone a range of similarity distances. This is found unpersuasive as Stanton et al. describe Table 2 (in caption) as containing results of nearest neighbors searches which clearly represent similarity distances. Each of the eleven examples in Table 2 clearly represent eleven sets of ranges. Stanton et al. describe original queries and additional hits in the caption of Table 2 which clearly represents the first molecules and subsequent compounds in each of the ranges, respectively. Applicants state that Table 2 discloses the hit percent for all compounds returned in the nearest neighbor search for each of the eleven disclosed examples. It is acknowledged that Table 2 discloses 11 nearest neighbor searches with each search representing a range, as stated in instant claim 3. Applicants state Figure 5b plots the hit percent for the combination of molecules from all eleven examples and does not disclose the hit percent as a function of nearest neighbor distance for each independent sample. This is acknowledged; however, the hit percent is clearly stated in Table 2 (last column) for each of the 11 example (ranges). Applicants state the hit percent in Stanton et al. is the hit percent for the molecules tested that have a given nearest neighbor distance from the original query. This is acknowledged. Applicants state there is no disclosure in Figure 5b or anywhere else in the Stanton et al. reference, that the hit percent for all molecules within the range between the original query and a given nearest neighbor distance. This is found unpersuasive as Table 2

clearly states this information with original queries and additional hits within each of the eleven nearest neighbor searches. The interpretation of "fractions-correctly-predicted metric" is described above in the 35 USC 102 rejection.

Applicants state Stanton et al. do not disclose the step of "counting the number of molecules away from said first molecule at which the fractions-correctly-predicted metric for said first molecule drops below a threshold value". Applicants also state Stanton et al. select a number of closest neighbors without specific criteria. This is found unpersuasive as Stanton et al. disclose a threshold of a NN distance of 1.9 or less in order to find a 20% hit rate (page 26, col. 1, lines 6-11). This represents a fractions-correctly-predicted metric (% hit rate) that is at 20% with values that are below a threshold value (1.9). Another example is seen in example 1 of Table 2 where a 10% hit rate has 4 compounds (counted number of molecules, third column) showing MICs of <= a particular threshold value. Applicants state that the hit rate in Stanton et al. is not the same as the claimed "fractions-correctly-predicted metric". This is found unpersuasive as the claimed "fractions-correctly-predicted metric", when interpreted as broadly and reasonably possible, does indeed encompass the hit rate in the Stanton et al. reference.

Applicants state Stanton et al. do not disclose the limitation of the "choosing" step in instant claim 3. This is found unpersuasive as Stanton et al. do contain passages that represent the claim limitations, as described in the 35 USC 102 rejection above. Applicants state that the hit rate in Stanton et al. is not the same as the claimed "fractions-correctly-predicted metric". This is found unpersuasive as the claimed "fractions-correctly-predicted metric", when interpreted as broadly and reasonably possible, does indeed encompass the hit rate in Stanton et

al. It is also noted that a portion of the "choosing" step in amended claim 3 is considered NEW MATTER which must be deleted in order to nullify the NEW MATTER rejection.

Applicants state that instant claim 3 would require additional steps, including "selecting a first molecule" from a "subset" created in the hierarchical cluster analysis and sorting all of the molecules from the "set" of the large combinatorial library "in descending order of numerical simlilarity". This is found unpersuasive as Applicants would not need to add other steps to their invention. Stanton et al. reads on claim 3 and the remainder of the instant invention because it discloses an embodiment species within the metes and bounds of instant claim 3 and the remainder of the instant invention, as fully described above. Applicants state Stanton et al. only depicts Euclidean distances in Figure 5 from original query compounds for compounds returned in the nearest neighbor searches, not for the entire combinatorial library of compounds. This is found unpersuasive as set and subsets can be found throughout the Stanton et al. reference. For example, the combinatorial library can be considered to be a set. Also, the entire list of compounds in Table 2 can be considered to be a set. Each example within Table 2 can be considered a subset. Due to the broad interpretation of words such as "set" and "subset", it appears that the Stanton et al. reference falls within the metes and bounds of the claimed invention.

Applicants state claim 7 requires a "repeating" step using "a plurality of different threshold values and minimum distances". This is acknowledged. Applicants state Stanton et al. do not disclose multiple threshold values for a "fractions-correctly-predicted metric". This is found unpersuasive as claim 7 does not mention the threshold values are for a "fractions-correctly-predicted metric". Also, Stanton et al. disclose that the hit rate can be controlled by

altering assay conditions used or setting rigorous criteria of a specific property (i.e. 80% inhibition instead of 50%) as well as looking at a broad range of hits (page 22, col. 1, lines 32-36) which is reasonably interpreted as repeating the count process with various thresholds. Applicants state Stanton et al. do not disclose the use of multiple minimum nearest neighbor distances. This is found unpersuasive as Stanton et al. disclose using minimum distances (see Table 2). Stanton et al. disclose a threshold of a NN distance of 1.9 or less (multiple distances) in order to find a 20% hit rate (page 26, col. 1, lines 6-11). It is also noted that instant claim 7 does not state that the minimum distances must be different.

Because the Applicants' arguments are deemed unpersuasive, the 35 USC 102 rejection is still deemed proper.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

April 6, 2004

ARDIN H. MARSCHEL
PRIMARY EXAMINER
4/12/04